Program for the Identification and Replacement of Endocrine Disrupting Chemicals

Douglas Young

US EPA

National Risk Management Research Laboratory

Cincinnati, OH

Project Outline

- Still in planning phase
- Develop a unique method for identifying potential EDC (external)
- Develop a program to aid in suggesting replacements for EDC (internal)
- If possible, combine into one software program

Identifying Potential EDC

- Use a QSAR type approach to quickly identify potential EDC (external)
- No duplication of concurrent efforts (such as COREPA and CoMFA)
- Use as another validation tool for concurrent efforts
- There is a Request for Proposals (RFP) to establish a collaborative agreement currently underway

Identifying Potential EDC cont'd

- Collaborator to be largely responsible for this portion of the project (Thesis or Dissertation work)
- We can help collect data needed to fill library

Replacement of Potential EDC

- Develop software that will aid in suggesting replacements for known or potential EDC (internal)
- Off shoot of the PARIS II Project (Program for Assisting the Replacement of Industrial Solvents)

PARIS II

- Suggests possible replacements for currently used solvents or solvent mixtures
- Uses the DIPPR (Design Institute for Physical Property Relationships) and UNIFAC to estimate 20 physical and chemical properties of the solvent(s) to be replaced
- Tries to find best match within database of over 1500 chemicals

PARIS II cont'd

- If it can't find a single replacement, it will allow the user to design a mixture
  - The user chooses the primary component and then the program will find the chemical that would form the best mixture
- If it can't find two component replacement, it will allow the user to add a 3rd chemical to the mixture
- Ad infinitum

EDC version of PARIS II

- The framework and coding are established
- Select key physical and chemical properties to satisfy the requirements for the specific EDC application

- Might not work with compounds that are designed to be pesticides & herbicides

Example

- Di(2-ethylhexyl)phthalate (DEHP)
  - Used as a plasticizer for PVC medical tubing
  - FDA has released a safety assessment on DEHP
  - Found that infants in certain circumstances may be exposed to unacceptable levels of DEHP
- Replacement outline
  - Describe qualities that are required for a plasticizer
  - Search the database for possible replacements

Example Cont'd

- Replacement Outline
  - Describe qualities that are required for a plasticizer
    - Plasticization Efficiency
    - Tensile strength
    - Vapor Pressure
    - Solubility
    - Toxicity
    - Viscosity
  - Match properties using components in database that have less potential for ED activity
  - Suggest a replacement or replacement mixture

Final Product

- A software program that will have a methodology to identify potential EDC and then will allow the user to design possible replacement chemicals (non potential EDC) based on desired properties

- Will be used as another validation tool to compliment the concurrent research projects

Timeline

- External
  - Determine collaborator during Winter of 2002
  - Project will begin Spring/Summer of 2002
  - Expected to last 3 years
- Internal
  - Post-doc already in place
  - Project began January of 2002
  - Expected to last 3 years